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## The 4% Solution (Approximately)

*To the Editor:*

Medical researchers spend a great deal of energy in measuring the frequencies of various disorders, signs, symptoms, and events. Yet, when they make statements about these frequencies, it sometimes appears that they are not thinking about how best to do it. A precise way to state a frequency is as a mean and SD or, less formally, as a mean with a verbal indication of its degree of imprecision, such as "about," "around," or "roughly." Instead, many authors seem reluctant to state a specific figure but prefer to state a range. For example, "2–3% of all couples are at high and recurrent risk of having a child with an inherited disease." (This and subsequent quotations are all taken from the published literature, but references are not given, for diplomacy's sake.) Or, again, "the frequency of congenital malformations is 3–5%." What does this mean? According to Humpty Dumpty it means whatever the writer means it to mean, nothing more and nothing less. But the writer does not say what she or he means it to mean.

Does it mean that the frequency is not lower than 3% and not greater than 5%? Probably not. Or that estimates of the frequency range from 3% to 5%? From what one knows of such estimates, this meaning also seems unlikely. Or that 3% and 5% are the confidence limits of the estimate of the mean? Again, probably not. What it really means, I fear, is that the writer can't make up his or her mind. It would be more charitable, perhaps, to say that the writer is unwilling to give a single figure because that would give a false impression of precision and is also reluctant to use an adjective implying imprecision, such as "about," "around," or, to sound more scientific, "approximately."

Some authors state frequencies as ranges to imply that the estimates vary widely. Fair enough. "The prevalence of sleepwalking is 1–6% of different patient populations" or, more striking, "hypopigmented patches occur in 15% to 85% of cases of tuberous sclerosis." "Depressive symptoms have been reported in 35–70% of post-viral fatigue patients." "Mild forms [of hyperstimulation syndrome] may be seen in 3–83% of women undergoing treatment." Not very helpful to the reader—or to the practitioner—but at least one gets the impression either that frequencies are vary variable or that estimates are very imprecise, or both. When the stated range is small, however, this cannot be the interpretation. "Klackenburg gives a prevalence rate of 5–6%." Or consider "a significant mortality rate of 0.5–1%." Surely these statements are not meant to imply a range but simply reflect a reluctance to state a single figure.

In contrast to those who feel impelled to state a range, others give a false sense of precision by stating a figure to an unrealistic number of decimal points. "Estimates [of the prevalence of sleepwalking] include 2.2% of young healthy adults, 2.5% of the general population, the highest being at age 11–12 (16.7%)." Do the figures after the decimal point mean anything?

Similarly for "a frequency of 1 in 42221 births," a figure presumably derived from letting the calculator complete the division, but do we really need that final 221 births? Does it not give a false sense of precision?

Some authors combine the two approaches. For example, "8.2% of CVS cases go on to amniocentesis. The risk of malformation is 2–3%." Or "the frequency [of x] is 3.5 to 15–20%." "The recurrence risk for autism is 8.6% with confidence limits of 5.8 to 12.2%" (what precision!); and the figure given for use in counseling is "8 to 9%"! Certain procedures for egg retrieval result in "an *average* of *about* 4–6 eggs per cycle" (emphasis mine). And some just don't seem to be paying attention. What does "at least 100 to 1000 cells" mean? Or "a frequency of approximately greater than 1%"? Or "in nearly 55.1% of . . . "? I could go on but hope I have made the point. Perhaps I am being finicky and pedantic, but when stating a frequency

why not think about the most meaningful way to do it?

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## Viability of Skin Biopsies Stored at −70°C

*To the Editor:*

In recent issues of the *Journal* the cryopreservation of lymphocytes before Epstein–Barr virus transformation was discussed (Louie and King 1991; Pressman and Rotter 1991). This led us to believe your readers may be interested in a technique for storing skin biopsies prior to establishment in culture, a technique which we have been using a for a number of years.

The possibility of storing small skin biopsies for a short time (2–3 wk) at −70°C has been reported by this laboratory (Fowler 1984). As stated then, a skin biopsy is taken at each postmortem performed at this hospital. It is not possible to set up cultures from all these biopsies, because of the cost and time involved. Biopsies are therefore collected into Eagle's basal medium (ICN Biomedicals) containing 10% FBS (Cytosystems) and antibiotics. Ten percent dimethyl sulfoxide is added, and the samples are transferred immediately to a −70°C freezer. In this study cultures were established as described in the previous report, after longer storage to determine the maximum storage time. The results are shown in table 1. It can be seen that, under the conditions used, viability is certain up to 6 mo.

**Table 1**

**Skin Biopsy Storage**

| Storage Time (mo) | No. of Biopsies Thawed | No. of Biopsies Growing |
|---|---|---|
| 3–4 | 6 | 6 |
| 5–6 | 6 | 6 |
| 7–8 | 6 | 5 |
| 9–10 | 8 | 0 |

This laboratory has stored about 200 biopsies each year for the past 6 years. Of these, 34 have been thawed and set up in culture, and 32 were successfully established.

The ability to store biopsies for up to 8 mo allows both time for the diagnosis of doubtful cases to be established and, if interests change, the chance to look at fibroblasts from conditions other than those currently being studied. This laboratory also stores excess tissue, if any, from biopsies being set up for culture, until such time as the cell line is successfully established. It may be possible to further extend the life of the skin biopsies stored in this way, by transferring them to a liquid nitrogen after overnight storage at −70°C.

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## The Cystic Fibrosis ΔF508 Mutation in the Albanian Population

*To the Editor:*

ΔF508 mutation is the most frequent cystic fibrosis (CF) allele in most European populations (Romeo and Devoto 1990). A collaborative study on 4,871 CF chromosomes in Europe (European Working Group